REMARKS

Pending claims

Claims 11-14, 16, 17, 19-31 and 47-52 are pending. No amendment is made with the present reply.

Rejections under 35 U.S.C. § 112, 1st Paragraph re Enablement

Claims 11-14, 16, 17, 19-31 and 47-52 stand rejected under 35 U.S.C. §112, first paragraph. The Examiner alleges that while the specification is enabled for the treatment of inflammation, hypertension and pain by the administration of spongosine and the amino acid gabapentin, it does not enable treatment of any of the other noted conditions with any other mixtures of spongosine and another analgesic agent as recited in claims 27 and 28.

The Examiner alleges that: the safety of spongosine with other analgesics is highly unpredictable; the "analgesic agent other than spongosine" defined in generic or subgeneric terms is too broad; only 2.5 pages of guidance are given showing how to treat pain associated with only a few model test hosts wherein the pain has been induced artificially; the specification contains only 1 example of combination of spongosine with gabapentin; and there is no guidance concerning how to safely select the "other" possible analgesics.

As a preliminary matter, Applicant notes that the rejected subject matter is recited in claims 27 and 28. Accordingly, the rejection is moot and should be withdrawn with respect to claims 11-14, 16, 17, 19-26, 29-31 and 47-52. Moreover, the rejection should be withdrawn for at least the following reasons.

Applicant has provided a working, in vitro example of combined administration with gabapentin, together with a statement applicable to the genus as a whole. Generally, Applicant's working, *in vivo* examples together with a statement applicable to the genus as a whole will ordinarily be sufficient to support enablement of the claimed genus. M.P.E.P. § 2164.02: "Proof of enablement will be required for other members of the claimed genus only where adequate reasons are advanced by the examiner to establish that a person skilled in the art could not use

the genus as a whole without undue experimentation." The Examiner acknowledges that Applicant's working, *in vivo* example of combined administration with gabapentin is enabling.

The Examiner's argument advances merely a conclusory allegation regarding safety issues, not reasoning supported by evidence. The Examiner advances no facts or reasoning to establish that a person skilled in the art could not use the genus as a whole without undue experimentation. Instead, Examiner concludes that alleged safety issues prevent Applicant's working, *in vivo* example from enabling *any* other combination of spongosine and an analgesic agent other than spongosine according to the claims. The Examiner does not provide any facts or evidence to support the alleged safety issue. Since the initial burden is on the examiner to give reasons for the lack of enablement, the examiner must also give reasons for a conclusion of lack of correlation for an *in vitro* or *in vivo* animal model example, such as the Examiner's conclusion of a lack of safety. A rigorous or an invariable exact correlation is not required, as stated in *Cross v. Iizuka*, 753 F.2d 1040, 1050, 224 USPQ 739, 747 (Fed. Cir. 1985). The Examiner's conclusory allegations about safety in the absence of any facts or reasoning are therefore not sufficient to support a lack of enablement.

One of ordinary skill will ordinarily administer and monitor drug levels for safety. As argued in previous responses, a person of ordinary skill is a pain physician, who is experienced in selecting among available analgesics and determining effective dosages. For example, according to the American Board of Pain Medicine's "Definition of Pain Medicine:"

> The specialty of Pain Medicine is concerned with the prevention, evaluation, diagnosis, treatment, and rehabilitation of painful disorders. Such disorders may have pain and associated symptoms arising from a discrete cause, such as postoperative pain or pain associated with a malignancy, or may be syndromes in which pain constitutes the primary problem, such as neuropathic pains or headaches. The diagnosis of painful syndromes relies on interpretation of historical data; review of previous laboratory, imaging, and electrodiagnostic studies; behavioral, social, occupational and avocational assessment; interview and examination by the pain specialist; and may require specialized diagnostic procedures, including central and peripheral neural blockade or monitored drug infusions. The special needs of the pediatric and geriatric populations are considered when formulating a comprehensive treatment plan for these patients. (Exhibit A, http://www.abpm.org/what/index.html, accessed October 28, 2007)

Since a pain physician may conduct "specialized diagnostic procedures, including central and peripheral neural blockade or monitored drug infusions," such a physician is experienced in administering combined drug infusions, e.g., a drug for central neural blockade and a drug for peripheral neural blockade, and in monitoring such infusions. Consequently, one of ordinary skill in the art can administer drug combinations, such as spongosine and an analgesic agent other than spongosine according to the claims.

Applicant respectfully submits that for at least the preceding reasons, the Examiner has not advanced adequate reasons to establish that a person skilled in the art could not use the genus as a whole without undue experimentation. Moreover, the rejection is moot and should be withdrawn with respect to claims 11-14, 16, 17, 19-26, 29-31 and 47-52. Consequently, the corresponding enablement rejection is improper. Applicant respectfully requests that the rejection be withdrawn.

Obviousness-type double patenting rejections

Claims 11-14, 16, 17, 19-31 and 47-52 stand provisionally rejected under the judicially created doctrine of obviousness type double patenting over claims 16-33 of co-pending Application Ser. No. 10/547,455, filed March 5, 2004, and claims 13-24 of co-pending Application Ser. No. 10/547,454, filed March 5, 2004.

The allegedly conflicting claims of Application Ser. Nos. 10/547,455 and 10/547,454, have not been patented. For this reason, the present rejection is a provisional obviousness-type double patenting rejection. Applicant will address any obviousness type patenting rejections upon notification that there are claims which are otherwise allowable.

Anticipation Rejection under 35 U.S.C. § 102(b)

Claims 11-14, 16, 17, 19-31 and 47-52 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Bartlett *et al.* J. Med. Chem. 1981, 24, 947-954 (Bartlett *et al.*) The Examiner alleges that Bartlett *et al.* disclose at Table I at page 949 and associated explanation at page 950, column 1, fifth full paragraph, that the administration of spongosine to treat carrageenan induced inflammation must have inherently included suppression of pain. The Examiner states that the

allegation of inherency is supported by the definition of "inflammation" in Taber's Cyclopedic Medical Dictionary, 19th Ed. (200 1) at page 1092, column 1, wherein the occurrence of "inflammation" is defined to include the simultaneous occurrence of' pain" and other symptoms.

Applicant respectfully submits that the inherent anticipation rejection is improper because inherency must be based on what was **necessarily** present in prior art, not what may be possible or probable.

The fact that a certain result or characteristic may occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic. *In re Rijckaert*, 9 F.3d 1531, 1534, 28 USPQ2d 1955, 1957 (Fed. Cir. 1993) (reversed rejection because inherency was based on what would result due to optimization of conditions, not what was necessarily present in the prior art); *In re Oelrich*, 666 F.2d 578, 581-82, 212 USPQ 323, 326 (CCPA 1981).

Further, "[t]o establish inherency, the extrinsic evidence 'must make clear that the missing descriptive matter is **necessarily** present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill. Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing **may** result from a given set of circumstances is not sufficient.'" *In re Robertson*, 169 F.3d 743, 745, 49 USPQ2d 1949, 1950-51 (Fed. Cir. 1999) (citations omitted, emphasis added).

The treatment of pain is not **necessarily** present in the experiments described by Bartlett *et al.* The experiments describe only treatment and measurement of swelling due to carageenan-induced edema as a model for inflammation. Bartlett *et al.* provides at p 953, column 2, last full paragraph: "Rat Paw Edema Test for Antiinflammatory Activity. Antiinflammatory activity was assessed by the inhibition of carrageenan-induced edema." Further, "Rats were dosed ... before measuring the thickness of both hind paws and the subplantar injection of 0.05 mL of carrageenan ...the ensuing swelling was measured, and the percent inhibition of the edema formation was calculated ..." (p 954, para 1, lines 5-10).[1]

Taber's Cyclopedic Medical Dictionary, 19th Ed. (2001) p 665-667 (Exhibit B) provides an extensive definition and discussion of edema. Nowhere does this definition recite pain, or

[1] By contrast, Applicant's carrageenan examples also included a separate pain stimulus (heat) and measurement of pain (paw withdrawal latency).

state that pain is a required or necessary component of edema. Therefore, edema does not necessarily require the presence of pain. Moreover, the only "anti-inflammatory activity" assessed by Bartlett et al. is a reduction in swelling, used to calculate "the percent inhibition of the edema formation." Therefore, the induction and treatment of carrageenan-induced edema by Bartlett *et al.* does not **necessarily** include the presence of pain, let alone the treatment of pain.

Therefore, the present claims are not inherently anticipated by Bartlett *et al.* Applicant respectfully requests that the corresponding rejection be withdrawn.

Obviousness Rejection under 35 U.S.C. § 103(a) re Co-pending Applications

Claims 11-14, 16, 17, 19-31 and 47-52 stand rejected under 35 U.S.C. § 103(a) as being obvious over co-pending Application Ser. Nos. 10/547,454 and 10/547,455. The Examiner alleges that these applications have claims that are obvious variations of the instant claims, "therefore rendering the instant claims obvious." The rejection also refers to the obviousness-type double patenting rejections for specific statements defining the bases for the findings of obviousness.

The present application, U.S. Pat. Appl. Ser. No. 10/537,564, was filed 8/28/06, and claims priority to PCT/GB2003/005379, filed 12/9/2003, and UK 0228723.3, filed 12/9/2002. Co-pending U.S. Pat. Appl. Ser. No. 10/547,455, was filed 7/26/2006, and claims priority to PCT/GB2004/000935, filed 3/5/2004, and UK 0305149.7, filed 3/7/2003. Co-pending U.S. Pat. Appl. Ser. No. 10/547,454, was filed 6/28/2006, and claims priority to PCT/GB2004/000952, filed 3/5/2004, and UK 0305150.5, filed 3/7/2003. Consequently, the present application has a priority date earlier than the co-pending applications.

Further, the present application and Application Ser. Nos. 10/547,454 and 10/547,455 were, at the time the claimed invention was made, owned by and subject to an obligation of assignment to Cambridge Biotechnology Ltd., the assignee of record for all three applications.

The rejection under 35 U.S.C. § 103(a) as being obvious over co-pending Application Ser. Nos. 10/547,454 and 10/547,455 is therefore improper. Applicant respectfully requests that it be withdrawn.

Obviousness Rejection under 35 U.S.C. § 103(a) re Bartlett *et al.* and Herrick-Davis *et al.*

Claims 11-14, 16, 17, 19-31 and 47-52 stand rejected under 35 U.S.C. § 103(a) as being obvious over Bartlett *et al.* in view of Herrick-Davis *et al.* European Journal of Pharmacology, 162 (1989) 365-369 (Herrick-Davis *et al.*). The Examiner alleges that Herrick-Davis *et al.* discloses that a variety of adenosine analogues that are also known in the art to be adenosine receptor agonists have been found to be analgesic agents with efficacy comparable to morphine. The Examiner alleges that one of the compounds tested, 2-chloroadenosine (CADO), is a close structural relative to spongosine. The Examiner alleges that the claims are obvious over Bartlett *et al.*, referring to the inherent anticipation rejection discussed in a preceding section, further in view of Herrick-Davis *et al.* The Examiner alleges that one of ordinary skill in the art would have been motivated to combine these references because both references are directed to disclosures of the analgesic effects observed following the administration of 2-substituted analogues of adenosine, including spongosine.

As the Examiner acknowledges, the Bartlett et al. reference did not specifically disclose the testing of spongosine to determine its analgesic activity. Moreover, as discussed above, Applicant respectfully submits that Bartlett et al. does not inherently anticipate the claimed invention because it does not inherently include pain or the treatment of pain. Therefore, one of ordinary skill in the art would not have been motivated to combine the cited references as alleged by the Examiner. The obviousness rejection over Bartlett *et al.* in view of Herrick-Davis *et al.* should be withdrawn for this reason alone.

Further, the Examiner's allegation that CADO is somehow closely analogous to spongosine is not supported because structural similarity does not give rise to obviousness in the absence of similar properties. As discussed in a previous reply, "it is not structural similarity alone that gives rise to obviousness, but the concomitant assumption that the structurally similar compounds will have like properties." *Ex Parte Chwang* 231 USPQ 751, 752 (Bd. Pat. App. & Int'f 1986). However, one of skill in the art would recognize that spongosine (2-methoxyadenosine) has a significantly different properties as compared to CADO, such as shape, dipole moment, etc. Moreover, as argued previously, compounds cited by the Examiner such as

CADO are shown in Ueeda *et al.* Life Sciences, Vol. 49, pp. 1351-1358 (Ueeda *et al.*) to have substantially different binding constants at A_1A and A_2A receptors as compared with 2-ethoxyadenosine. In particular, the inhibition constant K_i for 2-chloroadenosine (#3) at A_1AR differs from that for 2-ethoxyadenosine (#13) by a factor of 132 in rat and 170 in guinea pig. Furthermore, according to Ueeda *et al.*, 2-ethoxyadenosine (#13) is selective for the A_2AR receptor, whereas compounds including CADO (#3) are unselective (Ueeda, *et al.*, page 1354, lines 3-4). Consequently, because the Ueeda, *et al.* reference teaches that there are substantial differences between 2-ethoxyadenosine and CADO, one of ordinary skill in the art would not expect a 2-alkoxyadenosine such as spongosine (2-methoxyadenosine) to have similar properties to CADO. Contrary to the Examiner's allegation, one of ordinary skill in the art would not view CADO as closely analogous to spongosine. Thus, disclosure of CADO as an analgesic in Herrick-Davis et al. does not support an obviousness rejection of the claimed method of treating pain which comprises administering spongosine (2-methoxyadenosine) to a subject in need of such treatment.

For at least the preceding reasons, the rejection of claims 11-14, 16, 17, 19-31 and 47-52 under 35 U.S.C. § 103(a) as being obvious over Bartlett *et al.* in view of Herrick-Davis *et al.* is overcome. Applicant respectfully requests that the rejection be withdrawn.

CONCLUSION

For the reasons set forth above, Applicants submit that the claims of the instant application, as amended herein, are in condition for allowance. Reconsideration and withdrawal of the Examiner's objections and rejections are hereby requested. Allowance of the claims is earnestly solicited.

Please apply any required charges or credits to deposit account 06-1050, referencing attorney docket no. 13425-0170US1.

Respectfully submitted,

Date: Feb 19, 2009

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What is Pain Medicine?

Definition of Pain Medicine

The specialty of Pain Medicine is concerned with the prevention, evaluation, diagnosis, treatment, and rehabilitation of painful disorders. Such disorders may have pain and associated symptoms arising from a discrete cause, such as postoperative pain or pain associated with a malignancy, or may be syndromes in which pain constitutes the primary problem, such as neuropathic pains or headaches. The diagnosis of painful syndromes relies on interpretation of historical data; review of previous laboratory, imaging, and electrodiagnostic studies; behavioral, social, occupational and avocational assessment; interview and examination by the pain specialist; and may require specialized diagnostic procedures, including central and peripheral neural blockade or monitored drug infusions. The special needs of the pediatric and geriatric populations are considered when formulating a comprehensive treatment plan for these patients..

The pain physician serves as a consultant to other physicians but is often the principal treating physician and may provide care at various levels, such as direct treatment, prescribing medication, prescribing rehabilitative services, performing pain relieving procedures, counseling of patients and families, direction of a multidisciplinary team, coordination of care with other healthcare providers and consultative services to public and private agencies pursuant to optimal healthcare delivery to the patient suffering from a painful disorder. The pain physician may work in a variety of settings and is competent to treat the entire range of painful disorders encountered in delivery of quality health care.

EXHIBIT A

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20

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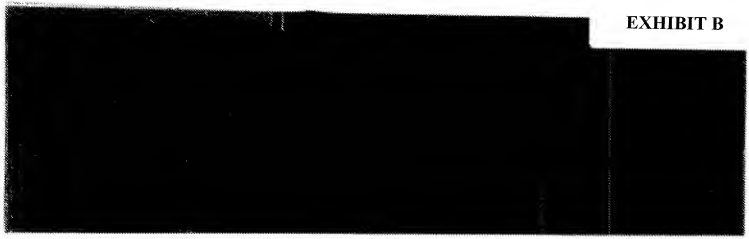

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OMOTIONAL CODE:

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h benign and malig

ek-top'ik) Ectopic

zm) [Gr. ektos, out- a, form, mold] The cell protoplasm. ec- stic (ĕk"tō-plăz'mik

ot'ō-mē) [Gr. ekto tome, incision] Re- ectopic pregnancy. -tĕr'i-goyd) [Gr. ek- ryx, wing, + eidos, external (lateral) brings the jaw for

[Gr. ektopos, dis- ent of an organ or pia

('ĭ-nă) [Gr. ektos, e, net] The outer

'sĭs) [" + osteon, ition] Formation of riosteum.

rm") [" + "] An ly temperature var- temperature of the opposite of endo- therm.

s) [" + thrix, hair] duces arthrospores

k"ō-trĭ-kŏf'ĭ-tŏn) [" hyton, plant] A for ophyton megalospo

n) [" + zoon, ani- nimal that lives on er animal.

miscarriage] Com- ng congenital ab

ō-dăk'tĭl-ĭzm) [" ismos, state of] of all or part of a

'lē-ă) [" + melos, f the long bones of

ē-lŭs [" melos, with ectromelia

[Gr. ek, out, + to complete or par- generally the eco

m) Eversion of an ie edge of an eyelid. es include aging or tin, scarring, infec- facial nerve.

ro-sin-dak'tĭ-le) [" dactylos, finger] of one or more fin- ingers are fused to-

[Gr. ekzein, to boil] c for an itchy red

rash that initially weeps or oozes serum and may become crusted, thickened, or scaly. Eczematous rash may result from various causes, including allergies, irritating chemicals, drugs, scratching or rubbing the skin, or sun exposure. It may be acute or chronic. The rash may become secondarily infected. SEE: *dermatitis*.

TREATMENT: Avoiding the cause of the rash (e.g., a sun-sensitizing drug; the leaves of the poison oak plant; an irritating soap or perfume) prevents recurrences and allows the skin to heal. Locally applied astringent solutions (such as Burow's solution), antihistamines, or corticosteroid ointments, tablets, or injections may relieve the inflammation.

PATIENT CARE: Patients are helped to identify and avoid allergens in their diet or environment. Clothing should be soft textured, preferably cotton, and washed in a mild detergent. Fingernails should be kept short to decrease damage from scratching. Antihistamines may help to reduce itching at night. Maintaining a room temperature below 72°F, using humidifiers during the winter, and bathing in tepid water help keep the skin hydrated and decrease itching. SEE: ***Nursing Diagnoses Appendix; Standard and Universal Precautions Appendix.***

asteatotic e. SYN: *winter itch.*

dyshidrotic e. Pompholyx.

erythematous e. Dry, pinkish, ill-defined patches with itching and burning; slight swelling with tendency to spread and coalesce; branny scaling; roughness and dryness of skin. This type may become generalized.

e. herpeticum Massive crops of vesicles that become pustular, occurring when herpes simplex virus infection occurs in a person, usually an infant, with pre-existing eczema. SYN: *Kaposi's varicelliform eruption.*

lichenoid e. Eczema with thickening of the skin.

nummular e. Eczema with coin- or ova-shaped lesions. It is often associated with dry skin and worsens in dry weather. SEE: illus.

NUMMULAR ECZEMA

pustular e. Follicular, impetiginous, or consecutive eczema including eczema rubrum (red, glazed surface with little oozing), eczema madidans (raw, red, and covered with moisture), eczema fissum (thick, dry, inelastic skin with cracks and fissures), squamous eczema (chronic on soles, legs, scalp; multiple circumscribed, infiltrated patches with thin, dry scales).

seborrheic e. Eczema marked by excessive secretion from the sebaceous glands. SYN: *seborrhea.*

vaccinatum e. The spreading of vaccinia virus to localized areas of skin, or to the entire body, in patients recently vaccinated against smallpox. This reaction is a rare complication of smallpox vaccination, occurring in about 40 per million of newly vaccinated individuals. It usually occurs in people with preexisting eczema and is occasionally fatal.

eczematous (ĕk-zĕm'ă-tŭs) Marked by or resembling eczema.

ED *effective dose; erythema dose.*

E.D. *Emergency Department.*

ED_{50} The median effective dose, producing the desired effect in 50% of subjects tested.

EDC *expected date of confinement.*

EDD *expected date of delivery.*

edema, oedema (ĕ-dē'mă) *pl.* **edemas** or **edemata** [Gr. *oidema*, swelling] A local or generalized condition in which the body tissues contain an excessive amount of tissue fluid. *Ascites* and *hydrothorax* are words for excess fluid in the peritoneal and pleural cavities, respectively. Generalized edema was previously termed dropsy. **edematous** (-ăt-ŭs), *adj.*

ETIOLOGY: Edema may result from increased permeability of the capillary walls; increased capillary pressure due to venous obstruction or heart failure; lymphatic obstruction; disturbances in renal function; reduction of plasma proteins; inflammatory conditions; fluid and electrolyte disturbances, particularly those causing sodium retention; malnutrition; starvation; or chemical substances such as bacterial toxins, venoms, caustic substances, and histamine.

TREATMENT: Bedrest helps relieve lower extremity edema. Dietary salt should be restricted to less than 2 g/day. Fluid intake may be restricted to about 1500 ml in 24 hr. This prescription may be relaxed when free diuresis has been attained. Diuretics relieve swelling when renal function is good and when any underlying abnormality of cardiac function, capillary pressure, or salt retention is being corrected simultaneously. One of various effective diuretics may be used. Diuretics are contraindicated in pre-eclampsia and when serum potassium levels are very low (e.g., less than 3.0 mEq/dl). They may be ineffective in cardiac edema associated with advanced renal insufficiency. The diet in edema should be adequate in protein, high in calories, and rich in vitamins. Patients with significant edema should weigh themselves daily to gauge fluid loss or retention.

PATIENT CARE: Edema is documented according to type (pitting, nonpitting, or brawny), extent, location, symmetry, and degree of pitting. Areas over bony prominences are palpated for edema by pressing with the fingertip for 5 sec, then releasing. Normally, the tissue should immediately rebound to its original contour, so the depth of indentation is measured and recorded. The patient is questioned about increased tightness of rings, shoes, waistlines of garments, belts, and so forth. Periorbital edema is assessed; abdominal girth and ankle circumference are measured; and the patient's weight and fluid intake and output are monitored. Fragile edematous tissues are protected from damage by careful handling and positioning and by providing and teaching about special skin care. Edematous extremities are mobilized and elevated to promote venous return, and lung sounds auscultated for evidence of increasing pulmonary congestion. Prescribed therapies, including sodium restriction, diuretics, ACE inhibitors, protein replacement, and elastic stockings or other elastic support garments, are provided, and the patient is instructed in their use.

angioneurotic e. Angioedema.

brain e. Swelling of the brain due to an increase in its water content. It may be caused by a variety of conditions, including increased permeability of brain capillary endothelial cells; swelling of brain cells associated with hypoxia or water intoxication; trauma to the skull; and interstitial edema resulting from obstructive hydrocephalus. SYN: *brain swelling; cerebral edema.*

e. bullosum vesicae A form of edema affecting the bladder.

cardiac e. Accumulation of fluid due to congestive heart failure. It is most apparent in the dependent portion of the body and/or the lungs.

cerebral e. Brain edema.

dependent e. Edema or swelling of the lower extremities or, if the patient is lying down, of the sacrum.

high-altitude pulmonary e. ABBR: HAPE. Pulmonary edema that may occur in aviators, mountain climbers, or anyone exposed to decreased atmospheric pressure. SEE: *hypoxia.*

inflammatory e. Edema associated with inflammation. The cause is assumed to be damage to the capillary en-

dothelium. It is usually nonpitting and localized, and red, tender, and warm.

laryngeal e. Swelling of the larynx, usually resulting from allergic reaction and causing airway obstruction unless treated. Therapy consists of intravenous or intratracheal epinephrine, emergency tracheostomy, or both.

malignant e. Rapid destruction of tissue by cutaneous or subcutaneous infections, such as anthrax or clostridial species.

e. neonatorum Edema in newborn, esp. premature, infants. This condition is usually transitory, involving the hands, face, feet, and genitalia, and rarely becomes generalized.

pitting e. Edema, usually of the skin of the extremities. When pressed firmly with a finger, the skin maintains the depression produced by the finger. SEE: illus.

PITTING EDEMA
Demonstration of pitting edema of the foot

pulmonary e. A potentially life-threatening accumulation of fluid in the interstitium and alveoli of the lungs. The collected fluid may block the exchange of oxygen and carbon dioxide and produce respiratory failure. SYN: *acute edema of lung*. SEE: *Nursing Diagnoses Appendix*.

ETIOLOGY: Fluid may seep out of the alveolar capillaries if these blood vessels are damaged and become excessively permeable to liquids (noncardiogenic pulmonary edema) or if hydrostatic pressures within blood vessels exceed the strength of the normal alveolar capillary wall (cardiogenic pulmonary edema). Cardiogenic pulmonary edema can result from any condition that causes congestive heart failure, including myocardial infarction, ischemia, or stunning; severe valvular heart disease; arrhythmias; excessive intravenous fluid administration; and diastolic dysfunction, among others.

Noncardiogenic pulmonary edema usually results from blood vessel injury, as occurs in the adult respiratory distress syndrome (sepsis, shock, aspiration pneumonia, airway obstruction). Occasionally protein-rich fluid floods the lungs as a result of drug exposure (e.g., heroin overdose), hypoalbuminemia, high-altitude exposure (mountain sickness), hemorrhage in or around the brain, or other conditions.

SYMPTOMS: Patients feel as though they are suffocating and often demonstrate labored, noisy breathing, cough productive of bloody sputum; air hunger; anxiety; palpitations; and altered mental status. Signs of the condition include a rapid respiratory rate, heaving of the chest and abdomen, intercostal muscle retractions, and cyanosis. To improve the movement of air into and out of the chest, the patient will often sit upright to breathe and resist lying down.

TREATMENT: Oxygen should be administered immediately. Morphine sulfate, nitrates, and loop diuretics are typically given to patients with cardiogenic pulmonary edema. Positive airway pressure ventilation or intubation and ventilator-assisted breathing may be required.

PROGNOSIS: The outlook is good if the condition is stabilized or reversed with treatment.

PATIENT CARE: The patient's head is elevated; respirations and ventilatory effort are assessed. Oxygen is administered as prescribed, with care taken to limit the flow-rate in patients whose respiratory drive is compromised. The lungs are auscultated for adventitious breath sounds, such as crackles, gurgles, and wheezes, and the heart is assessed for apical rate and gallops. The patient is monitored for a cough productive of pink, frothy sputum. His or her skin is checked for diaphoresis and pallor or cyanosis. A medication history is collected, especially for cardiac or respiratory drugs and use of recreational drugs. The patient's cardiac rate and rhythm, blood pressure, and oxygen saturation levels are monitored continuously. An intravenous (IV) line administering normal saline solution (NSS) is inserted at a keep-vein-open rate to provide access for medication administration. Prescribed first-line drug therapy is administered, and the patient's response to the drugs is evaluated. IV morphine slows respirations, improves hemodynamics, and reduces anxiety. It should be administered prior to initiating continuous positive air pressure (CPAP). CPAP, in turn, improves oxygenation and decreases cardiac workload, thus decreasing the need for intubation and ventilation with positive end-expiratory pressure (PEEP). An indwelling urinary catheter is inserted to accurately monitor the patient's fluid status; diuresis should begin within 30 minutes of administration of an IV loop

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tender, and warm.
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rom allergic reaction
y obstruction unless
consists of intrave-
cheal epinephrine
stomy, or both.
rapid destruction of
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nthrax or clostridial

Edema in newborn,
ants. This condition
tory, involving the
and genitalia, and
eralized.
, usually of the skin
When pressed firmly
in maintains the de-
by the finger. SEE

EDEMA
ng edema of the foot

A potentially life-
dation of fluid in the
lveoli of the lungs
may block the ex-
and carbon dioxide
atory failure. SYN:
. SEE: *Nursing Di-*

may seep out of the
f these blood vessels
become excessively
ds (noncardiogenic
or if hydrostatic
lood vessels exceed
normal alveolar cap-
ogenic pulmonary
pulmonary edema
ny condition that
eart failure, includ-
retion, ischemia, or
vular heart disease;
ssive intravenous
; and diastolic dys-
ers.
pulmonary edema
blood vessel injury,
ult respiratory dis-
osis, shock, aspira-
rway obstruction;

occasionally protein-rich fluid floods the lungs as a result of drug exposure (e.g., heroin overdose), hypoalbuminemia, high altitude exposure (mountain sickness), hemorrhage in or around the brain, or other conditions.

SYMPTOMS: Patients feel as though they are suffocating and often demonstrate labored, noisy breathing; cough productive of bloody sputum; air hunger; anxiety; palpitations; and altered mental status. Signs of the condition include a rapid respiratory rate, heaving of the chest and abdomen, intercostal muscle retractions, and cyanosis. To improve the movement of air into and out of the chest, the patient will often sit upright to breathe and resist lying down.

TREATMENT: Oxygen should be administered immediately. Morphine sulfate, nitrates, and loop diuretics are typically given to patients with cardiogenic pulmonary edema. Positive airway pressure ventilation or intubation and ventilator-assisted breathing may be required.

PROGNOSIS: The outlook is good if the condition is stabilized or reversed with treatment.

PATIENT CARE: The patient's head is elevated; respirations and ventilatory effort are assessed. Oxygen is administered as prescribed, with care taken to limit the flow-rate in patients whose respiratory drive is compromised. The lungs are auscultated for adventitious breath sounds, such as crackles, gurgles, and wheezes, and the heart is assessed for apical rate and gallops. The patient is monitored for a cough productive of pink, frothy sputum. His or her skin is checked for diaphoresis and pallor or cyanosis. A medication history is collected, especially for cardiac or respiratory drugs and use of recreational drugs. The patient's cardiac rate and rhythm, blood pressure, and oxygen saturation levels are monitored continuously. An intravenous (IV) line administering normal saline solution (NSS) is inserted at a keep-vein-open rate to provide access for medication administration. Prescribed first-line drug therapy is administered, and the patient's response to the drugs is evaluated. IV morphine slows respirations, improves hemodynamics, and reduces anxiety. It should be administered prior to initiating continuous positive air pressure (CPAP). CPAP, in turn, improves oxygenation and decreases cardiac work load, thus decreasing the need for intubation and ventilation with positive end-expiratory pressure (PEEP). An indwelling urinary catheter is inserted to accurately monitor the patient's fluid status; diuresis should begin within 30 minutes of administration of an IV loop diuretic. Pulmonary edema is a true respiratory emergency that terrifies the patient. All individuals involved with the patient through this crisis must remain as calm and quiet as possible, provide ongoing reassurance, and validate everything occurring through basic and simply understood explanations. Health care providers should discuss with the patient his or her feelings about the episode and give more in-depth explanations of what occurred. The at-risk patient is taught early warning signs to act on immediately, in an effort to prevent future episodes.

purulent e. Swelling caused by a local collection of pus.

salt-induced e. A form of edema worsened by excess sodium in the diet.

edematogenic (ē-dĕm″ă-tō-jĕr′ĭk) Causing edema.

edentia (ē-dĕn′shē-ă) [L. e, without, + *dens*, tooth] Absence of teeth.

edentulous (ē-dĕnt′ū-lŭs) Without teeth.

edetate calcium disodium (ĕd′ĕ-tāt) The disodium salt of ethylenediaminetetra-acetic acid. A chelating agent, it is used in diagnosing and treating lead poisoning. Trade names are Calcium Disodium Versenate and Versene CA.

edetate disodium (ĕd′ĕ-tāt dī-sō′dē-ŭm) A chelating agent, disodium dihydrogen ethylenediaminetetra-acetate dihydrate. It is used to treat hypercalcemia.

edge A margin or border.

bevel e. A tooth edge produced by beveling.

cutting e. An angled or sharpened edge for cutting, as an incisor tooth or the blade of a knife.

denture e. The margin or border of a denture.

incisal e. The sharpened edge of a tooth produced by occlusal wear; the labiolingual margin.

edible (ĕd′ĭ-bl) [L. *edere*, to eat] Suitable for food; fit to eat; nonpoisonous.

edrophonium chloride (ĕd″rō-fō′nē-ŭm) A cholinergic drug. Trade name is Tensilon. SEE: *edrophonium test.*

edrophonium test The use of edrophonium chloride to test for the presence of myasthenia gravis. The appropriate dose is injected intravenously; if there is no effect, a larger dose is given within 45 sec. A positive test demonstrates brief improvement in strength unaccompanied by lingual fasciculation. The test may also be used to determine an overdose of a cholinergic drug. An excessive dose of cholinergic drug produces weakness that closely resembles myasthenia. A very small dose of edrophonium chloride given intravenously worsens the weakness if it is due to cholinergic drug overdose and improves it if it is due to myasthenia gravis.

CAUTION: The test should not be performed unless facilities and staff for respiratory resuscitation are immediately available.

EDTA *ethylenediaminetetra-acetic acid.*

eduction (ē-dŭk′shŭn) [L. e, out, + *ducere*, to lead] Emergence from a particular state or condition (e.g., coming out of the effects of general anesthesia). SEE: *induction* (4).

Edwards' syndrome (James H. Edwards, U.S. geneticist, b. 1928) Trisomy 18.

EE *coefficient of elastic expansion.*

EEE *eastern equine encephalitis.*

EEG *electroencephalogram.*

EENT *eyes, ears, nose, and throat.*

EEOC *Equal Employment Opportunity Commission.*

EFA *essential fatty acid.*

effacement (ē-fās′mĕnt) In obstetrics, the thinning of the cervix as the internal os is slowly pulled up into the lower uterine segment.

effect (ĕ-fĕkt′) [L. *effectus*, to accomplish] The result of an action or force. Particular effects are listed under the first word. SEE: *cumulative effect; Doppler effect; side effect.*

effectiveness (ē-fĕk′tĭv-nĕs) The ability to cause the expected or intended effect or result.

effective radiating area ABBR: ERA. The area of a therapeutic ultrasound head that produces useful ultrasonic energy, measured in square centimeters (cm^2). The effective radiating area is calculated by identifying all points where the ultrasonic energy is at least 5% of the maximum measured intensity at the transducer's surface.

effector (ē-fĕk′tor) Any organ stimulated by motor nerve impulses, a muscle that contracts or a gland that secretes. SYN: *effector organ.*

effector cell An active cell of the immune system responsible for destroying or controlling foreign antigens. SEE: *leukocyte.*

effector organ Effector.

effeminate (ē-fĕm′ĭ-năt) Pert. to a male who has the physical characteristics or mannerisms of a female.

effemination (ē-fĕm″ĭ-nā′shŭn) [L. *effeminare*, to make feminine] The production of female physical characteristics in a male. SYN: *feminization.*

efferent (ĕf′ĕr-ĕnt) [L. *efferens*, to bring out] Carrying away from a central organ or section, as efferent nerves, which conduct impulses from the brain or spinal cord to the periphery; efferent lymph vessels, which convey lymph from lymph nodes; and efferent arterioles, which carry blood from glomeruli of the kidney. Opposite of afferent.

effervesce (ĕf″ĕr-vĕs′) [L. *effervescere*, to